

FIGURE 1A

FIGURE 2A

CCCGACTGGTCGAAAGACAGGACAGACTTGAAACAGGGGGACAGCTCCTGGCGAAACGAAGACGTGGAGGTTTTACCAGGGATAAGAAG 90 AAAAGACACCTTCCTAGTGAGCAGCTGCCCAGCTCCTGCTCAGTTTTGCCTCGGGGTAGCACCTCCAGCCACAGAAAGACAAGCAGCTGGTAAG 180 TCTCTCCAGGTAGGACTTGCTGCAACCCAGCTGCTGGACTGAACCGGGACTTTGCATACTCTCCGAAGTATGGTGAGTTGGTGCT 270 HVSVC CACTTCAAAGTTGCCTGGTGAAGGAAGATAAGGTCGATCGCAGAGACTAAGGGGGAGAGGCGCTGCTCCTCTTCTCCCCACCAAG 360 CCACAATCACCAACATCTGTCAGAGGETCTGGGAGTACCTAGAACCCTATCTCCCCTGTTTGTCCAEGGAGGCAGACAAGTCAACCGTGA 450 M S N I C O R L W E Y L E F Y L F C L S T E A D K S T Y I ENPGALCSPOSORHGHY FV_ALFDYOARTA aggacttgagcttccgagcaggtgacaaacttcaagttctggacactttgcatgagggctggtggtttgccagacacttggagaaaagac 630 ${
m SH}$ ${
m S}$ GAGATGGCTCCAGTCAGCAACTACAAGGCTATATTCCTTCTAACTACQTGGCTGAGGACAGAAGCCTACAGGCAGAGCCGTGGTTCTTTG 720 R D G S S Q Q L Q G Y I P S N Y V A E D R S L Q A E P W F F #**ĞAQCAATCQGAAG**ATCAGATGCAQAGAAACAACTATTATATTCAQAAAACAAGACCQGTTCCTTTCTAATCAGAGAAAGTGAAAGCCAAA # 810 F A I G R S D A E K O L L Y S E N K T G S F L I R E S E S O SH2 AAGGAGAATTCTCTCTTTCAGTTTTAGATGGAGCAGTTGTAAAACACTACAGAATTAAAAGACTGGATGAAGGGGGATTTTTTCTCACGC 900 K G E F S L S V L D G A V V K H Y R I K R L D E G G F F L T R R R I F S T L N E F V S H Y T K_IT 5 D G L C V K L G K P C OBOL DAKAPTOTTODADA TADOTDAKODODABATABABABDAKAADABBTDODAKAKATATDOTBTTTABTTTADOTDBADODTBBADATÉ **LKIOVPAPFDLSYKTVDOWEIDRNSIQLLK** CATTGGGATCTGGTCAGTTTGGCGAAGTATGGGAAGGTCTGTGGAACAATACCACTCCAGTAGCAGTGAAAACATTAAAACCAGGTTCAA 1170 RLGSGQFGEYWEGLWNNTTPYAYKTLKPGS TEGATCCAAATGACTTCCTGAGGGAGGCACAGATAATGAAGAACCTAAGACATCCAAAGCTTATCCAGCTTTATGCTGTTTGCACTTTAG 1260 <u>H D P N D F L R E A Q I H K N L R H P K L I Q L Y A V C T L</u> AAGATCCAATTTATATTATTACAGAGTTGATGAGACATGGAAGTCTGCAAGAATATCTCCAAAAATGACACTGGATCAAAAATCCATCTGA 1350 <u>E</u>D P I Y I I T E L K R K G S Ł Q E Y L O N D T G S K I H L CTCAACAGGTAGACATGGCGGCACAGGTTGCCTCTGGAATGGCCTATCTGGAGTCTCGGAACTACATTCACAGAGATCTGGCTGCCAGAA 1440 TQOYDHAAQVASGHAYLESRNYIHRDLAAR ATGTCCTCGTTGGTGAACATAATATCTACAAAGTAGCAGATTTTGGACTTGCCAGAGTTTTTAAGGTAGATAATGAAGACATCTATGAAT 1530 N Y L Y G E H N I Y K V A D F G L A R V F K V D N E D I Y E CTAGACACGAAATAAAGCTGCCGGTGAAGTGGACTGCGCCCGAAGCCATTCGTAGTAATAAATTCAGCATTAAGTCCGATGTATGGTCAT 1820 S R H E I K L P V K W T A P E A 1 R S N K F S I K S D V W S TTGGAATCCTTCTTTATGAAATCATTACTTATGGCAAAATGCCTTACAGTGGTATGACAGGTGCCCAGGTAATCCAGATGTTGGCTCAAA 1710 <u>FGILLYEI</u>ITYGKMPYSGMTGAQYIQMLAO ACTATAGACTTCCGCAACCATCCAACTGTCCACAGCAATTTTACAACATCATGTTGGAGTGCTGGAATGCAGAGCCTAAGGAACGACCTA 1800 N Y R L P Q P S N C P Q Q F Y N L K L E C W N A E P K E R P

FIGURE 3A

43

Expression of MKK1 and MKK2

		MKK1	MKK2
Human			
	Meg-01	+++	+++
Meg/Eryth	K562	++	+
	Mo7e-	++	+
	HEL	+++	++
	KG-1	+	++
Myelo/Mac	HL-60	+	+
	TF-1	+	+
	ALL-1	-	+
B-cell	Raji	-	-
	Daudi	-	-
	Molt-3	-	-
T-cell	Jurkat	-	-
Epithelial	Hela	-	-
Roden	t		
	ВМ	+	+++
	Spleen	+++	+
	Thymus	•	-
•	Liver	-	-
	Brain	+	-
rat neural	P19	+	- ·

Immunoprecipitation Of In Vitro Transcribed Translated MKK1 And MKK2 Proteins

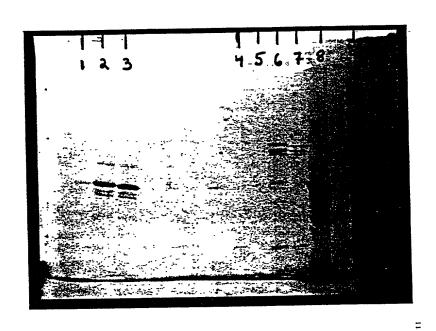
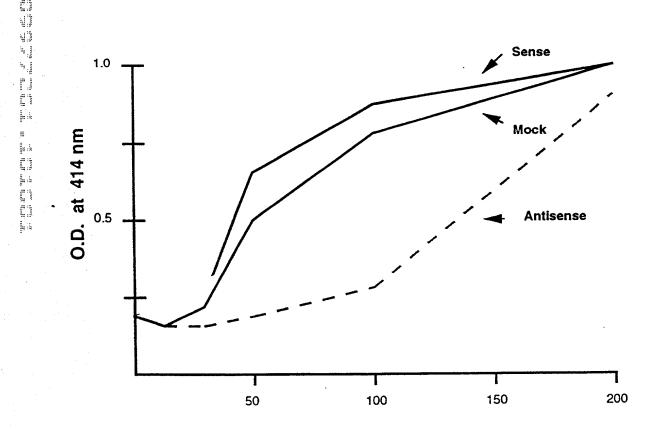


FIGURE 5

Antisense MKK1 Expression Suppresses AChE Production In Primary Murine Bone Marrow Cultures



Cell Number x 10³/200 ul

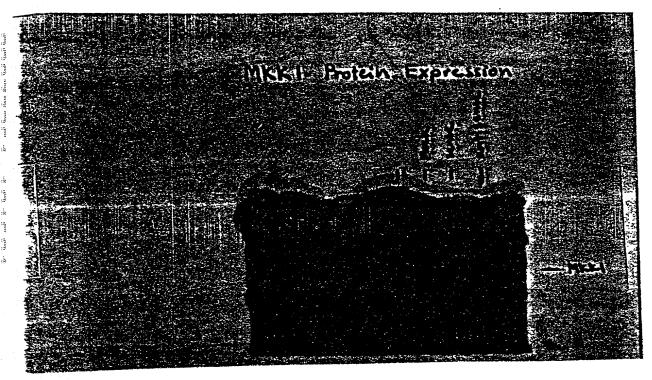


FIGURE 6B

MKK2 AND MKK3 AUTOPHOSPHORYLATE TRANSPHOSPHORYLATE PROTEINS WHEN EXPRESSED IN BACTERIA

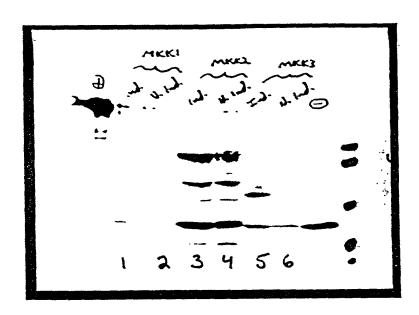


FIGURE 7

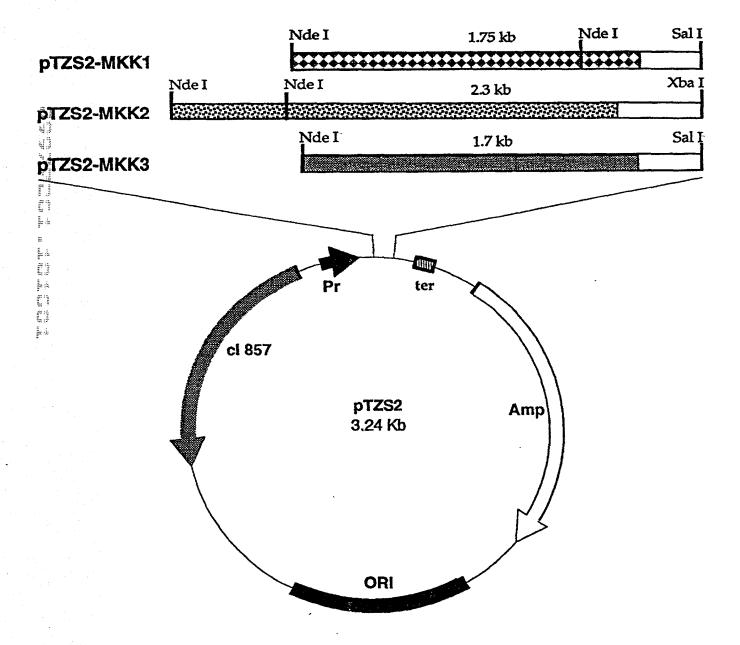


FIGURE 8

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MAGRGSLVSWRAFHGCDSAEELPRVSPRFL MKK1 aa
                                ---- hCSK (JH0559)
61 RPKPGELAFRKGDVVTILEACENKSWYRVK MKK1 aa
22 GTAEQDLPFCKGDVLTIVAVTKDPNWYKAK hCSK (JH0559)
91 HHTSGOEGLLAAGALREREALSADPKLSLM MKK1 aa
52 NKV-GREGIIPANYVQKREGVKAGTKLSLM hCSK (JH0559)
121 PWFHGKISGOEAVOOLOPPEDGLFLVRESA MKK1 aa
81 PWFHGKITREQAERLLYPPETGLFLVREST hCSK (JH0559)
151 RHPGDYVLCVSFGRDVIHYRVLHRDGHLTI MKK1 aa
111 NYPGDYTLCVSCDGKVEHYRIMYHASKLSI hCSK (JH0559)
181 DEAVFFCNLMDMVEHYSKDKGAICTKLVRP MKK1 aa
141 DEEVYFENLMQLVEHYTSDADGLCTRLIKP hCSK (JH0559)
211 KRKHGTKSAEEELARAGWLLNLOHLTLGAO MKK1 aa
171 KVMEGTVAAQDEFYRSGWALNMKELKLLQT hCSK (JH0559)
241 I G E G E F G A V L O G E Y L G O K V A V K N I K C D V T A MKK1 aa
201 I G K G E F G D V M L G D Y R G N K V A V K C I K N D A T A hCSK (JH0559)
271 QAFLDETAVMTKMOHENLVRLLGVILHO-- MKK1 aa
231 QAFLAEASVMTQLRHSNLVQLLGVIVEEKG hCSK (JH0559)
GLYIVMEHVSKGNLVNFLRTRGRALVNTAO MKK1 aa
261 GLYIVTEYMAKGSLVDYLRSRGRSVLGGDC hCSK (JH0559)
129 LLOFSLHVAEGMEYLESKKLVHRDLAARNI MKK1 aa
291 LLKFSLDVCEAMEYLEGNNFVHRDLAARNV hCSK (JH0559)
359 LVSEDLVAKVSDFGLAKAERKGLDSSRLPV MKK1 aa
321 LVSEDNVAKVSDFGLTKEASSTQDTGKLPV hCSK (JH0559)
389 KWTAPEALKHGKFTSKSDVWSFGVLLWEVF MKK1 aa
351 KWTAPEALREKKFSTKSDVWSFGILLWEIY hCSK (JH0559)
419 SYGRAPYPKMSLKEVSEAVEKGYRMEPPEG MKK1 aa
381 SFGRVPYPRIPLKDVVPRVEKGYKMDAPDG hCSK (JH0559)
 449 C P G P V H V L M S S C W E A E P A R R P P F R K L A E K L MKK1 aa
411 C P P A V Y E V M K N C W H L D A A M R P S F L Q L R E Q L h CSK (JH0559)
 479 A R E L R S A G A P A S V S G O D A D G S T S P R S O E P MKK1 aa
 441 EH-----L hCSK (JH0559)
```

FIGURE 9

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MDTKSILEELLLKRSQQKKKMSPNNYKERL MKK2 aa
MAA-VILESIFLKRSQQKKKTSPLNFKKRL hAtk (X58957)
MNNFILLEEQLIKKSOOKRRTSPSNFKVRF hTKT (L10717)
1
1
1
                                                                                                               mTec (X5663)
      FVLTKTNLSYYE - - YDKMKRGSRKGSIEIK MKK2 aa
FLLTVHKLSYYEYDFERGRRGSKKGSIDVE hAtk (X58957)
FVLTKASLAYFEDR - - HGKKRTLKGSIELS hTKT (L10717)
31
30
31
                                                                            - - - - - - - mTec (X5663)
      59
60
59
4
       78
90
70
                ----- SFPVKINFHSSP----- Q mTec (X5663)
98 SRSOWLKALOKEIRGNPHLLVKYHSGFFVD MKK2 aa
120 LRKRWIHOLKNVIRYNSDLVQKYHPCFWID hAtk (X58957)
98 SRQRWVLALKEETRNNNNSLVPKYHPNFWMD hTKT (L10717)
17 SRDRWVKKLKEEIKNNNNIMIKYHPKFWAD mTec (X5663)
128 G K F L C C Q Q S C K A A P G C T L W E A Y A N L H T A V N MKK2 aa
150 G Q Y L C C S Q T A K N A M G C Q I L E N R N G S L K P G S hAtk (X58957)
128 G K W R C C S Q L E K L A T G C A Q Y D - - - - - - P hTKT (L10717)
47 G S Y Q C C R O T E K L A P G C E K Y N L F E S S I - - - mTec (X5663)
150 E E K H R V PT F P D R V L K I P R A V P V L K M D A P S S MKK2 aa

180 S H R K T K K P L P P - - - T P E E D Q I L K K P L P P E hAtk (X58957)

140 T K N A S K K P L P P - - - T P E D N R - - - - - - hTKT (L10717)

73 - - - - - R K T L P P - - - A P E - - - I K K R R P P - mTec (X5663)
188 S T T L A Q Y DNE S K K N Y G S Q P P S S S T S L A Q Y D MKK2 aa

206 PA A A P V S T S E L K K - - - - - - - - - V V A L Y D hAtk (X58957)

166 - - - R P L WE P E E T V - - - - - - - - V T A L Y D hTKT (L10717)

89 P P I P P E E N T E E I - - - - - - - V V A M Y D mTec (X5663)
218 SNSKKIYGSOPNFNMOYIPREDFP-DWWQV MKK2 aa
225 YMPMNANDLOLRKGDEYFILEESNLPWWRA hAtk (X58957)
182 YOTNDPQELALRRNEEYCLLDSSEIHWWRV hTKT (L10717)
108 FOATEAHDLRLERGQEYIILEKNDLHWWRA mTec (X5663)
 247 RKLKSSSSEDVASSNQKERNVNHTTSKIS MKK2 aa
255 RD--KNGQEGYIPSNYVTE-A----- hAtk (X58957)
212 QD--RNGHEGYVPSSYLVEKS----- hTKT (L10717)
138 RD--K----- MTec (X5663)
 307 EQLLRQKGKEGAFMVRNSSQVGMYTVSLFS MKK2 aa
292 EQLLKOEGKEGGFIVRDSSKAGKYTVSVFA hAtk (X58957)
250 EKLLLDTGKEGAFMVRDSRTAGTYTVSVFT hTKT (L10717)
154 EOLLRTEDKEGGFMVRDSSOPGLYTVSLYT mTec (X5663)
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```
337 K - AVNDK KGTVKHYHVH - - TNAENKLYLAE MKK2 aa
322 KST-GDPQGVIRHYVVY - - CSTPQSQYYLAE hAtk (X58957)
280 KAVVSENNPCIKHYHIKETNDNPKRYYVAE hTKT (L10717)
184 KFG-GEGSSGFRHYHIKETATSPKKYYLAE mTec (X5663)
364 NYCFDSIPKLIHYHQHNSAGMITRLRHPVS MKK2 aa
349 KHLFSTIPELINYHQHNSAGLISRLKYPVS hAtk (X58957)
310 KYVFDSIPLLINYHOHNGGGLVTRLRYPVC hTKT (L10717)
213 KHAFGSIPEIIEYHKHNAAGLVTRLRYPVS mTec (X5663)
394 TKANKVPDSVSLGNGIWELKREEITLLKEL MKK2 aa
379 QQNKNAPSTAGLGYGSWEIDPKDLTFLKEL hAtk (X58957)
340 FGRQKAPVTAGLRYGKWVIDPSELTFVQEI hTKT (L10717)
243 TKGKNAPTTAGFSYDKWEINPSELTFMREL mTec (X5663)
424 GSGQFGVVQLGKWKGQYDVAVKMIKEGSMS MKK2 aa
409 GTGQFGVVKYGKWRGQYDVAIKMIKEGSMS hAtk (X58957)
370 GSGOFGLVHLGYWLNKDKVAIKTIREGAMS hTKT (L10717)
273 GSGLFGVVRLGKWRAQYKVAIKAIREGAMC mTec (X5663)
454 E D E F F Q E A Q T M M K L S H P K L V K F Y G V C S K E Y MKK2 aa
439 E D E F I E E A K V M M M L S H E K L V Q L Y G V C T K Q R hAtk (X58957)
400 E E D F I E E A E V M M K L S H P K L V Q L Y G V C L E Q A hTKT (L10717)
303 E E D F I E E A K V M M K L T H P K L V Q L Y G V C T Q Q K mTec (X5663)
 484 PIYIVTEYISNGCLLNYLRSHGKGLEPSQL MKK2 aa
469 PIFIITEYMANGCLLNYLREMRHRFQTQOL hAtk (X58957)
430 PICLVFEFMEHGCLSDYLRTQRGLFAAETL hTKT (L10717)
333 PIYIVTEFMERGCLLNFLRQRQGHFSRDML mTec (X5663)
 514 LEMCYDVCEGMAFLESHQFIHRDLAARNCL MKK2 aa
499 LEMCKDVCEAMEYLESKOFLHRDLAARNCL hAtk (X58957)
460 LGMCLDVCEGMAYLEEACVIHRDLAARNCL hTKT (L10717)
363 LSMCQDVCEGMEYLERNSFIHRDLAARNCL mTec (X5663)
  VDRDLCVKVSDFGMTRYVLDDQYVSSVGTK MKK2 aa
529 VNDQGVVKVSDFGLSRYVLDDEYTSSVGSK hAtk (X58957)
490 VGENQVIKVSDFGMTRFVLDDQYTSSTGTK hTKT (L10717)
393 VNEAGVVKVSDFGMARYVLDDQYTSSSGAK mTec (X5663)
  FPVKWSAPEVEHYEKYSSKSDVWAFGILMW MKK2 aa

559 FPVRWSPPEVLMYSKFSSKSDIWAFGVLMW hAtk (X58957)

520 FPVKWASPEVFSFSRYSSKSDVWSFGVLMW hTKT (L10717)

423 FPVKWCPPEVFNYSRFSSKSDVWSFGVLMW mTec (X5663)
   604 EVFSLGKOPYDLYDNSOVVLKVSOGHRLYR MKK2 aa
589 EIYSLGKMPYERFTNSETAEHIAOGLRLYR hAtk (X58957)
550 EVFSEGKIPYENRSNSEVVEDISTGFRLYK hTKT (L10717)
453 EIFTEGRMPFEKNTNYEVVTMVTRGHRLHR mTec (X5663)
   PHLASDTIYOIMYSCWHELPEKRPTFQQLL MKK2 aa
619 PHLASEKVYTIMYSCWHEKADERPTFKILL hAtk (X58957
580 PRLASTHVYOIMNHCWKERPEDRPAFSRLL hTKT (L10717
483 PKLATKYLYEVMLRCWQERPEGRPSFEDLL mTec (X5663)
                                                                                                                                                                hAtk (X58957)
                                                                                                                                                                htkt (L10717)
    664 SSIE PLREK DKH
649 SNIL DVM DEES
610 RQLAEIAES --- GL
513 RTIDE LVECEET FGR
                                                                                                                                                                 MKK2 aa
                                                                                                                                                                 hAtk (X58957)
                                                                                                                                                                  htkt (L10717)
                                                                                                                                                                  mTec (X5663)
```

```
1
1
1
1
1
1
1
11
    SGYRYGTDPTPQHYPSFGVTSIPN--YNNFhFynPPSQYDPDPT-OLSGAF--THIPD--FNNFcYrkGGGAFPASOTPSKPASADGHRGPSAAFAPAhSrcSVSHYGAEPTTVSPCPSSSAKGTAVNFSSLhYesAADHYGPDPTKARPAS-SFAHIPN--YSNFhFyrTIYVRDPTSNKQQRPVPESQLLPGQRFQTKhLynPVYVPDPTSTIKPGPNSHNSNTPGIR----hHck
                                                                 - Y L E P MKK3 MPI aa
26
26
28
28
30
30
28
     PIVPLDGKGTLLIRNGSEVRD-PLVTYEGS hLck
26
     PLPPLVVFNHLAPPSPNQ - -
31
15
     Y L P C L S T E A D K S T V I E N P G A L C S P Q S Q R H G MKK3 MPI aa
H A A - - - G G Q G L T V F G G V N - - S S S H T G T L R T hFyn
H A A - - - A V S P P V P F S G P G F Y P C N T L Q A H S S cYrk
A A E P - - - - - - K L F G G F N S S D T V T S P Q R A G hSrc
54
51
58
    58
57
60
54
55
49
45
               ---YFVALFDYQARTAEDLSFRAGDK MKK3 MPI aa
    79
88
60
64
69 LQVLDTLHEGWWFARHLEKRRDGSSQQLQG MKK3 MPI aa
109 FOILNSSEGDWWEARSLTTGETG----- hFyn
108 FHIINNTEGDWWEARSLSSGATG-----
                                                                               cYrk
111 LOIVNNTEGDWWLAHSLSTGOTG------
118 FOIINNTEGDWWEARSIATGKNG-----
                                                                               hSrc
                                                                               hYes
104 FHILNNTEGDWWEARSLSSGKTG-
90 MKVLEEH-GEWWKAKSLLTKKEG-
84 MVVLEES-GEWWKARSLATRKEG-
88 LRILEQS-GEWWKAOSLTTGQEG-
79 LOVLRST-GDWWLARSLVTGREG-
                                                                               hLyn
                                                                               hLck
                                                                               mBlk
```

FIGURE 11A

```
Y I P S N Y V A E D R S L Q A E P W F F G A I G R S D A E K MKK3 MPI aa
Y I P S N Y V A P V D S I Q A E E W Y F G K L G R K D A E R hFyn
Y I P S N Y V A P V D S I Q A E E W Y F G K I G R K D A E R CYRK
Y I P S N Y V A P S D S I Q A E E W Y F G K I T R R E S E R hSrc
99
132
131
134
141 Y I P S N Y V A PAD S I Q A E E W Y F G KMG R K D A E R
127 CIPSNYVAPVDSIOAEEWYFGKIGRKDAER hFgr

112 FIPSNYVAKLNTLETEEWFFKDITRKDAER hLyn

106 YIPSNYVARVDSLETEEWFFKGISRKDAER hLck

110 FIPFNFVAKANSLEPEPWFFKNLSRKDAER hLck

101 YVPSNFVAPVETLEVEKWFFRTISRKDAER mBlk
129 Q L L Y S ENKTG S F L I R E S E S Q K G E F S L S V L D MKK3 MPI aa
162 Q L L S F G N P R G T F L I R E S E T T K G A Y S L S I R D hFyn
161 Q L L C H G N C R G T F L I R E S E T T K G A Y S L S I R D cYrk
164 L L L N A E N P R G T F L V R E S E T T K G A Y C L S V S D hSrc
171 L L L N P G N Q R G I F L V R E S E T T K G A Y S L S I R D hYes
157 Q L L S P G N P Q G A F L I R E S E T T K G A Y S L S I R D hFgr
142 Q L L A P G N S A G A F L I R E S E T L K G S F S L S V R D hLyn
136 Q L L A P G N M L G S F M I R D S E T T K G S Y S L S V R D hLck
140 Q L L A P G N T H G S F L I R E S E S T A G S F S L S V R D hLck
131 Q L L A P M N K A G S F L I R E S E S N K G A F S L S V K D mBlk
                               --- GAVVKHYRIKRLDEGGFFLTRRRIF MKK3 MPI aa
     1
  192 W D D M K G D H V K H Y K I R K L D N G G Y Y I T T R A Q F
191 W D E A K G D H V K H Y K I R K L D S G G Y Y I T T R A Q F
   159
                                                                                                                                                                                                                           hFyn
                                                                                                                                                                                                                            cYrk
                FDNAKGLNVKHYKIRKLDSG GFY I TSRTQ F
                                                                                                                                                                                                                            hSrc
  194 FDNAKGLNVKHYKIKKLDISGGETTTISKIVT INSTE

201 W D E I R G D N V K H Y K I R K L D N G G Y Y I T T R A Q F hYes

187 W D Q T R G D H V K H Y K I R K L D M G G Y Y I T T R V Q F hFgr

192 F D P V H G D V I K H Y K I R S L D N G G Y Y I S P R I T F hLyn

166 Y D P R Q G D T V K H Y K I R T L D N G G F Y I S P R S T F hHck

170 F D Q N Q G E V V K H Y K I R N L D N G G F Y I S P R I T F hLck

161 I T T - Q G E V V K H Y K I R S L D N G G Y Y I S P R I T F mBlk
   194
    184 STLNEFVSHYTKTSDGLCVKLGKPCLKIQV MKK3 MPI aa
222 ETLQQLVQHYSERAAGLCCRLVVVPCHKGM - hFyn
221 DTIQQLVQHYIERAAGLCCRLAVPCPKGT - cYrk
224 NSLQQLVAYYSKHADGLCHRLTTVCPTSK - hSrc
231 DTLQKLVKHYTEHADGLCHKLTTVCPTVK - hYes
217 NSVQELVQHYMEVNDGLCNLLIAPCTIMK - hFgr
202 PCISDMIKHYQKQADGLCRRLEKACISPK - hLyn
196 STLQELVDHYKKGNDGLCOKLSVPCMSSK - hHck
200 PGLHELVRHYTNASDGLCTRLSRPCQTQK - hLck
190 PTLQALVOHYSKKGDGLCOKLTLPCVNLA - mBlk
                  PAPFDLSYKTVDQWEIDRNSIQLLKRLGSG MKK3 MPI aa
PRLTDLSVKTKDVWEIPRESLQLIKRLGNG hFyn
PKLADLSVKTKDVWEIPRESLQLLQKLGNG CYRK
PQTQGLA---KDAWEIPRESLRLEVKLGQG hSrc
PQTQGLA---KDAWEIPRESLRLEVKLGQG hYes
PQTLGLA---KDAWEISRSSITLERRLGTG hFgr
       214
       251
       250
       253
       260
                    PQ - - - KPWDKDAWEIPRESIKLVKRLGAG hLyn
PQ - - - KPWEKDAWEIPRESLKLEKKLGAG hHck
PO - - - KPWWEDEWEVPRETLKLVERLGAG hLck
PK - - - NLWAQDEWEIPRQSLKLVRKLGSG mBlk
        246
        231
        225
```

FIGURE 11B

```
QFGEVWEGLWNNTTPVAVKTLKPGSMDPND MKK3 MPI aa
244
     QFGEVWMGTWNGNTKVAIKTLKPGTMSPES hFyn
281
280 OFGEVWMGTWNGTTKVAVKTLKPGTMSPEA cYrk
280 CFGEVWMGTWNGTTRVAIKTLKPGTMSPEA hSrc
     CFGEVWMGTWNGTTKVAIKTLKPGTMMPEA hYes
CFGDVWLGTWNGSTKVAVKTLKPGTMSPKA hFgr
273
    QFGEVWMGYYNN STKVAVKTLKPGTMSVQA hLyn
QFGEVWMATYNKHTKVAVKTMKPGSMSVEA hHck
QFGEVWMGYYNGHTKVAVKSLKQGSMSPDA hLck
QFGEVWMGYYKNNMKVAIKTLKEGTMSPEA mBlk
257
251
255
245
274 F LREAQIMKNLRHPKLIQLYAVCTLEDPIY MKK3 MPI aa
     FLEEAQIMKKLKHDKLVQLYAVVS-EEPIY
311
     FLEEAQIMKRLRHDKLVQLYAVVS-EEPIY
310
     FLQEAQVMKKLRHEKLVOLYAVVS-EEPIY
310
     FLOEAQIMKKLRHDKLVPLYAVVS-EEPIY
317
     FLEEAOVMKLLRHDKLVOLYAVVS-EEPIY
FLEEANLMKTLQHDKLVRLYAVVTREEPIY
FLAEANVMKTLQHDKLVKLHAVVTKE-PIY
FLAEANVMKTLQHQRLVKLHAVVT-QEPIY
303
287
281
                                                                                     hLck
     FLGEANVMKTLQHERLVRLYAVVTRE-PIY mBlk
    IIT ELM R HG S LQ E Y LQ NDTG S K I H LTO Q V D MKK3 MPI aa I V T E Y M N K G S L L D F L K D G E G R A L K L P N L V D h Fyn I V T E F M S Q G S L L D F L K D G D G R Y L K L P Q L V D cYrk I V T E Y M S K G S L L D F L K G E T G K Y L R L P Q L V D h S r c I V T E F M S K G S L L D F L K E G D G K Y L K L P Q L V D h Y es I V T E F M C H G S L L D F L K N P E G Q D L R L P Q L V D h F g r I I T E Y M A K G S L L D F L K S D E G G K V L L P K L I D h L y n I I T E F M A K G S L L D F L K S D E G S K Q P L P K L I D h H c k I I T E Y M E N G S L V D F L K T P S G I K L T I N K L L D h L c k I V T E Y M A R G C L L D F L K T D E G S R L S L P R L I D m B l k
304
340
339
339
346
 332
 317
 310
 314
 304
334 MAAQVASGMAYLESRNYIHRDLAARNVLVG MKK3 MPI aa
     MAAQVAAGMAYIERMNYIHRDLRSANILVG hFyn
 369 MAAQIAAGMAYIERMNYIHRDLRAANILVG
                                                                                     cYrk
369 MAAQIAS GMAY WERMNY WHRDLRAANILV G hSrc
     MAAQIADGMAYIERMNYIHRDLRAANILVG hYes
 376
 362 MAAQVAEGMAYMERMNYIHRDLRAAN<u>I</u>LVG hFgr
347 FSAQIAEGMAYIERKNYIHRDLRAANULVS hLyn
340 FSAQIAEGMAFIEQRNYIHRDLRAANILVS hHck
344 MAAQIAEGMAFIEERNYIHRDLRAANILVS hLck
 334 M S A O V A E G M A Y I E R M N S I H R D L R A A N I L V S mBlk
 364 EHNIYKVADFGLARVFKVDNEDIYESRHEI MKK3 MPI aa
400 NGLICKIADFGLARLI---EDNEYTARQGA hFyn
399 DNLVCKIADFGLARLI---EDNEYTARQGA CYrk
399 ENLVCKVADFGLARLI---EDNEYTARQGA hSrc
      ENLVCKIADFGLARLI - - EDNEYTARQGA hYes
 406
      ERLACKIADFGLARLI - - - KDDEYNPCOGS hFgr
 392
      ESLMCKIADFGLARVI - - - EDNEYTAREGA hLyn
ASLVCKIADFGLARVI - - - EDNEYTAREGA hHck
DTLSCKIADFGLARLI - - - EDNEYTAREGA hLck
ETLCCKIADFGLARII - - - DSEYTAQEGA mBlk
 377
 370
```

FIGURE 11C

```
MKK3 MPI aa
    KLPVKWTAPEAIRSNKFSIKSDVWSFGILL
     KFPIKWTAPEAALYGRFTIKSDVWSFGILL
                                                                                  hFyn
    KFPIKWTAPEAALFGKFTIKSDVWSFGILL CYrk
KFPIKWTAPEAALYGRFTIKSDVWSFGILL hSrc
426
426
    KFPIKWTAPEAALYGRFTIKSDVWSFGILQ hYes
     KFPIKWTAPEA<u>AL</u>FG<u>R</u>FTIKSDVWSFGILL
    K F P I K W T A P E A I N F G C F T I K S D V W S F G I L L
                                                                                  hLyn
    KFPIKWTAPEA IN FGSFTIKSDVWSFGILL
397
    KFPIKWTAPEAINYGTFTIKSDVWSFGILL hLck
KFPIKWTAPEAIHFGVFTIKADVWSFGVLL mBlk
401
390
424 YEIITYGKMPYSGMTGAQVIQMLAQNYRLP MKK3 MPI aa
457 TELVTKGRVPYPGMNNREVLEQVERGYRM P hFyn
    TELVTKGRVPYPGMNNREVLEQVERGYRMQ cYrk
TELTTKGRVPYPGMVNREVLDQVERGYRMP hSrc
463 TELVTKGRVPYPGMVNREVLEQVERGYRMP hYes
449 TELITKGRIPYPGMNKREVLEQVERGYRMP hYes
434 YEIVTYGKIPYPGMNKREVLEOVEQGYHMP hFgr
434 YEIVTYGRIPYPGMSNPEVIRALERGYRMP hLyn
427 MEIVTYGRIPYPGMSNPEVIRALERGYRMP hHck
431 TEIVTHGRIPYPGMSNPEVIRSLEHGYRMP mBlk
    QPSNCPQOFYN-IMLECWNAEPKERPTFET MKK3 MPI aa
CPQDCPISLH-ELMIHCWKKDPEERPTFEY hFyn
CPGGCPPSLH-DVMVQCWKREPEERPTFEY cYrk
454
487
486
486 C P P E C P E S L H - D L M C O C W R K E P E E R P T F E Y
493 C P Q G C P E S L H - E L M N L C W K K D P D E R P T F E Y
479 C P P G C P A S L Y - E A M E O T W R L D P E E R P T F E Y
                                                                                   hFor
     RVENCPDELY-DIMKMCWKEKAEERPTFDY
                                                                                   hLyn
464
457 RPENCPEELY-NIMMRCWKNRPEERPTFEY hHck
461 RPDNCPEELY-QLMRLCWKERPEDRPTFDY hLck
450 CPETCPPELYNDIITECWRGRPEERPTFEF mBlk
                                                                                   MKK3 MPI aa
 483 LRWKLEDYFE-TDSSYSDANNFIR
 516 LQSFLEDYFTATEPQYQPGEN
                                                                                   hFyn
 515 LQSFLEDYFTATEPQYQPGDN
515 LQAFLEDYFTSTEPQYQPGEN
                                                                                   cYrk
                                                                                   hSrc
522 IQSFLEDYFTATEPQYQPGEN
508 LQSFLEDYFTSAEPQYQPGDQ
493 LQSVLDDFYTATEGQYQQ--Q
486 IQSVLDDFYTATEGQYQQ--Q
490 LRSVLEDFFTATEGQYQP--Q
480 LQSVLEDFYTATEGQYEL--Q
                                                                                   hYes
                                                                                   hFgr
                                                                                   hLyn
                                                                                   hHck
                                                                                   hLck
                                                                                   mBlk
```

FIGURE 11D

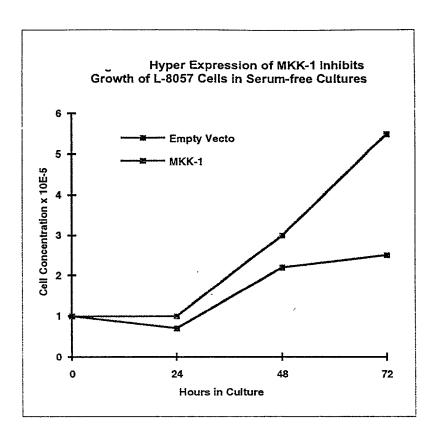


FIGURE 12

Growth Factor Response of MKK-1 Expressing L-8057 Cells

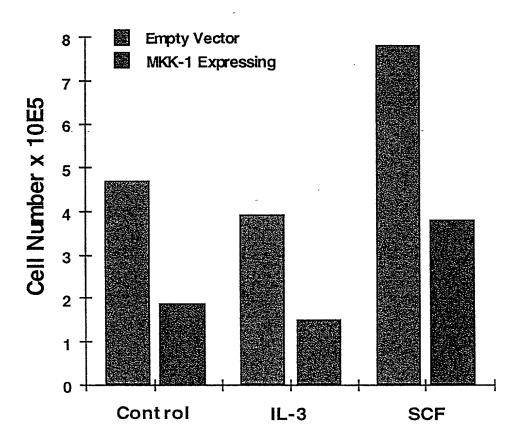


FIGURE 13

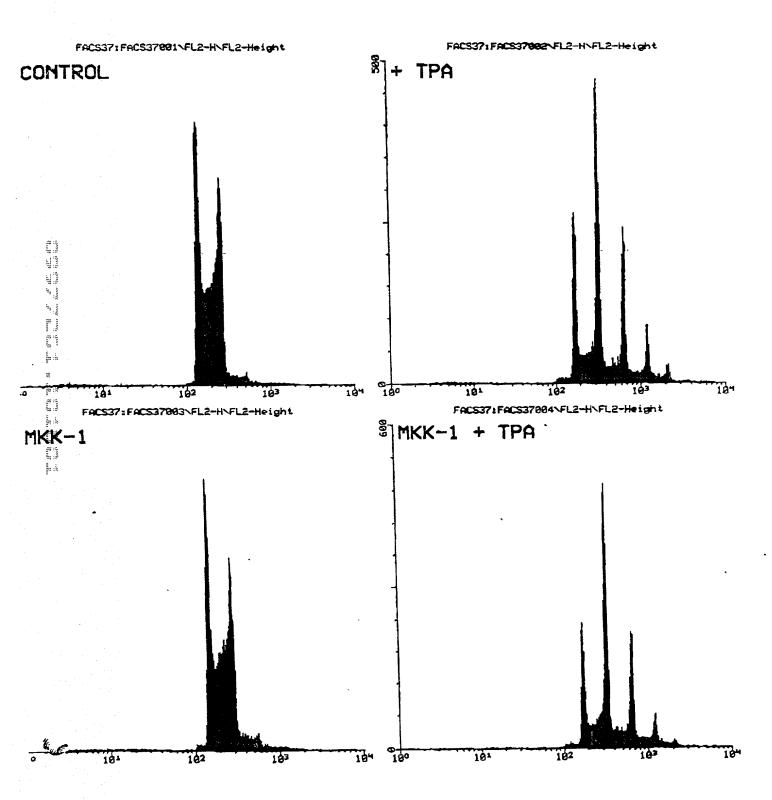


FIGURE 14